Tet1 controls meiosis by regulating meiotic gene expression.

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Public Summary:
This study examined the role of a key gene Tet1 in the development of femail primordial germ cells, and showed that Tet1's primary function is on the regulation of meiotic cell division.

Scientific Abstract:
Meiosis is a germ-cell-specific cell division process through which haploid gametes are produced for sexual reproduction. Before the initiation of meiosis, mouse primordial germ cells undergo a series of epigenetic reprogramming steps, including the global erasure of DNA methylation at the 5-position of cytosine (5mC) in CpG-rich DNA. Although several epigenetic regulators, such as Dnmt3l and the histone methyltransferases G9a and Prdm9, have been reported to be crucial for meiosis, little is known about how the expression of meiotic genes is regulated and how their expression contributes to normal meiosis. Using a loss-of-function approach in mice, here we show that the 5mC-specific dioxygenase Tet1 has an important role in regulating meiosis in mouse oocytes. Tet1 deficiency significantly reduces female germ-cell numbers and fertility. Univalent chromosomes and unresolved DNA double-strand breaks are also observed in Tet1-deficient oocytes. Tet1 deficiency does not greatly affect the genome-wide demethylation that takes place in primordial germ cells, but leads to defective DNA demethylation and decreased expression of a subset of meiotic genes. Our study thus establishes a function for Tet1 in meiosis and meiotic gene activation in female germ cells.